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EXAMINER	
LUCAS, ZACHARIAH .	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,002	BUKH ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *9,10 and 19-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6-8 and 11-17* is/are rejected.

7)☒ Claim(s) *2,3,5 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/3/01, 11/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-8 and 11-18) in the reply filed on September 29, 2005 is acknowledged.

2. Claims 9, 10, and 19-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 29, 2005.

3. Claims 1-8, and 11-18 are under consideration.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on December 3, 2001 and November 21, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Specification

5. The specification is objected to for containing referring to sequences without also identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). See, Figures, 3, 4, 6, and 7. The examiner would like to bring the applicant's attention to the following excerpt from MPEP §2422.03:

> 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. This requirement is also intended to permit references, in both the description and claims, to sequences set forth in the "Sequence Listing" by the use of assigned sequence identifiers without repeating

> the sequence in the text of the description or claims. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Where a sequence is embedded in the text of an application, it must be presented in a manner that complies with the requirements of the sequence rules.

The applicant is therefore required to amend the specification to comply with 37 CFR 1.821(d).

It is noted that SEQ ID NO: 1 of the present application does not appear to correspond to any of the GBV-B sequences specifically referred to in the application. In particular, the sequence varies from the GBV-B sequence referred to in Table 1 (page 24) in at least positions 1030, 1498, 1628, and 2552. However, the sequence also varies from the sequences of GVB-B 2/94 and pGBB in positions 2566 and 9067.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 6 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. This claim reads on an RNA transcript of a DNA construct comprising a nucleic acid encoding GBV-B. Because the GBV-B virus is a RNA virus, claim 6 reads on the GBV viral genome. Thus, the reference reads on non-statutory subject matter.

It is suggested that the claim be amended to read on an "isolated RNA transcript."

8. Claims 7 and 8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on "A cell" comprising the described nucleic acids. The art indicates that the B virus was originally discovered in a human, and that human cells may be infected by GBV. Thus, the claims as drafted read on embodiments wherein the cells are human cells. Further, as the claims do not require that the cells are isolated, the claims read on humans comprising such cells. Thus, the claims read on non-statutory subject matter.

It is suggested that the claims are amended to read on "An isolated cell."

9. Claims 11-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on GBV-B viruses produced by a cell expressing, or comprising the nucleic acid of, claim 1. Claim 1 reads on any isolated nucleic acid encoding GBV-B. Thus, claims 7, 8, and 13 read on GBV-B encoded by and comprising any GBV-B genomic/encoding sequence, which would include naturally occurring GBV-B viruses. The claims are therefore rejected as reading on non-statutory subject matter.

10. Claim 14 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on GBV-B viruses produced by a cell expressing, or comprising the nucleic acid of, claim 3. Claim 3 describes a nucleic acid of SEQ ID NO: 1. However, there is no information in the application indicating whether SEQ ID NO: 1 represents a naturally occurring GBV sequence, except that claim 3 indicates that the sequence encodes a GVB-B. Thus, for the purposes of this rejection, it is assumed that SEQ ID NO: 1 is a

naturally occurring sequence, and that therefore a virus comprising the sequence as its genome is a product of nature. Claim 14 is therefore rejecting as reading on non-statutory subject matter.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 4, 6-8. 11-13, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus of polynucleotides comprising any nucleic acid molecule encoding GB virus-B (GBV-B) and capable of expressing the virus when transfected into a cell.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the rejected claims broadly read on any isolated nucleic acid molecules which encodes GBV-B, and which molecules are capable of expressing the virus when transfected into cells. These claims describe the claimed genus through the identification of two functional limitations. First, the nucleic acid must encode a GB virus-B. Second, the nucleic acid molecule must be capable of expressing the virus when transfected into cells. The claims do not provide any structural requirements for the claimed nucleic acids.

As was indicated in the MPEP excerpt above, identification of a claimed genus only by its function is not sufficient descriptive support where the application does not also identify some other non-functional (e.g. structural) feature that correlates with the required function. In the present application, there is no description in the application as to what such minimal regions required for the activity are. While the application teaches that the additional 3' sequence referred to above is necessary, it does not teach what residues or structures within that sequence are required. Nor does the application teach that the 3' sequence is sufficient for the expression of the virus, or provide any structural identification of other regions of the viral genome that are required in addition to the newly identified 3' sequence. Thus, the functional language in the present claims is insufficient to demonstrate possession of the claimed genus.

It is noted that the specification teaches the sequence of a consensus GBV-B, and modified form thereof (comprising a mutation at nucleic acid position 7138), and provides a

number of additional 3' GBV-B NTR sequences (Figure 3) over what was previously thought in the art to be the complete GBV-B genome. The application teaches that these 3' sequences are necessary for the construction of infective GBV-B nucleic acid clones (i.e., clones capable of expressing the virus when transfected into cells). See, App., page 8 and Example 3. Thus, the application does provide multiple examples of nucleic acid sequences that may be included in the claimed sequences.

However, the courts have indicated that even the disclosure of multiple species within a claimed genus does not necessarily demonstrate possession of the genus, particularly where there is uncertainty in the art. See, In re Smyth, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973) (stating "where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus or combination claimed at a later date in the prosecution of a patent application."); and University of California v. Eli Lilly and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support). Thus, where there are indications in the art that one in the art would be uncertain as to the operability of undisclosed species, the disclosure of even a plurality of species within the claimed genus would not necessarily be sufficient to demonstrate possession of the claimed genus.

The art teaches that the art of protein modification is unpredictable. See e.g., Bowie et al. Science, 247:1306-10. Further, it is known that modifications to a viral genome, including PRRSV, can affect both the activity of certain viral proteins and have effects on viral replication. See e.g., Yoo et al., Vet Immunol Immunopathol 102: 143-54, abstract. In addition, other teachings in the art indicate that changes within a viral sequence are similarly unpredictable, with

even simple substitutions resulting in mutations having no effect, improving viral replication, or resulting in the inability to produce a viable virus. See e.g., U.S. 2003/0054505 at pages 18-19 (paragraphs [0163]-[0168]), and 20 (Table II). From such teachings, it is apparent that modifications to viral genomes are equally unpredictable absent teachings relating to the association of a modified sequence to the viral activities or those of the viral proteins.

In the present case, while the application provides several GBV 3' sequences, there is no description in the application as to what the minimal regions required for the claimed activities are. The application teaches that the additional 3' sequence referred to above is necessary, but it does not teach what residues or structures within that sequence are required. Nor does the application teach that the 3' sequence is sufficient for the expression of the virus, or provide any structural identification of other regions of the viral genome that are required in addition to the newly identified 3' sequence. Thus, the present application does not provide the necessary teachings identifying those residues or regions in the viral genome required for the claimed functions such that those in the art would know what modifications may be made to the genomic sequence without a loss of function. Because the application does not provide such teachings, there is insufficient written description support in the application for the presently claimed genus of nucleic acid molecules.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 8, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Simons et al. (PNAS 92: 3401-05). Claim 8 reads on a cell transfected with RNA encoding the GBV-B virus. However, the GBV-B virus is an RNA virus, and upon infection delivers RNA encoding itself into the host cell. Thus, claim 8 reads on a cell infected by GBV-B. Claims 11-13 each read on GBV-B viruses produced by cells transfected with a nucleic acid encoding the virus. As there would be no difference between such viruses and those produced in nature, these claims read on any GBV virus. Simons teaches serum containing the GBV-B virus, and therefore anticipates claims 11-13. Page 3401. The reference also teaches the infection of tamarins with the virus. Id. Because the reference teaches the infection of tamarins with the virus, and as such infection would inherently result in the insertion of viral RNA into a cell, the reference inherently teaches a cell according to claim 8. The claims are therefore rejected as anticipated by Simons.

Conclusion

15. No claims are allowed. Claims 2, 3, 5, and 18 are objected to as depending from rejected claims.

16. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

U.S. 2004/0039187 (Martin et al), and U.S. 6,627,437 (Traboni). Each of these references is considered relevant in that they each teach polynucleotides capable of expressing a GBV-B virus when transfected into cells. I.e., like the present application, each of these references also teaches a polynucleotide including the necessary 3' NTR

sequence for viral propagation. However, the references are not cited as art against the present claims because:

The Martin reference is not prior art in that it claims priority back to the same priority date as the present application.

The Traboni reference claims priority back to a foreign application filed on May 27, 1999, but is not applicable as prior art as of the earlier foreign application date. However, it is also noted that certain claims of this reference fall within the scope of, or overlap with, the scope of the inventions claimed in claims 1, 7, and 8 of the present application. See e.g., claims 1, 8, and 9 of the reference.

WO 95/21922 (of record in the December 2001 IDS). This reference is considered relevant because, like other art references, it purports to disclose the complete GBV genomic sequence. However, a comparison of the sequences of this reference with those of the present application indicate that the sequences in the art lack the required 3' NTR of the full-length sequence required for GBV production.

Bukh et al., Virology 262:470-78 (of record in the December 2001 IDS). This reference is considered relevant in that the reference includes the teachings of the present application, and names two of the present inventors as authors. However, the teachings of the reference vary from those of the present application in certain specific details found in the Table (Table 1) presented on page 473 of the reference are different from those of Table 1 on page 24 of the present application. In particular, the reference indicates that a cytosine rather than an thymine is found at position 2566 of the GVB-B 2/94 and pGBB sequences, and that the bases identified in the Table on page 24 of the application as corresponding to position 9067 actually correspond to position 9061.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 12/26/05